REMARKS

This application is amended in a manner to place it in condition for allowance at the time of the next Official Action.

Status of the Claims

Claims 21, 27-30, 32, 33, 35-37 and 40 are amended:

- Claim 21 specifies that the active ingredient is a pharmaceutically active ingredient (see, e.g., page 6, lines 10-11 of the present specification) and that the emulsion is a single emulsion (p. 8, l. 13-14; p. 9, l. 3).
- Claim 22 is amended to correct a translation mistake, i.e., the expression “the majority of" has been deleted. As currently amended claim 22 now corresponds to claim 2 as filed in the corresponding PCT application.
- Claims 27-29 and 33 specify that the active ingredients is a pharmaceutically active ingredient.
- Claims 35 and 36 no longer recite the expression "internal and/or external"
- Claim 37 has been amended to be consistent with claim 21, i.e., the expression “calibration by” has been replaced by "controlled”.
- Claim 40 depends from claim 21, and refers to the pharmaceutically active ingredient.

Claims 34 and 39 are cancelled without prejudice.

Claims 21-33, 35-38 and 40 remain in this application.

Restrictions

The pending claims are solely directed to Group I concerning a method of preparing microspheres.

Claim Objections

Claims 22-24 were objected to for being of improper dependent for failing to further limit the subject matter of a previous claim. The position of the Official Action was that claim 21 includes the limitation of biodegradable polymer, and that claim 22 (and thus claims 23 and 24) fails to further limit claim 21 because it recites "the microspheres are constituted in majority by the biodegradable polymer".

However, claim 21 recite that the phase comprises an active ingredient and a biodegradable polymer, and that microspheres are obtained. There is no relative a mount of biodegradable polymer specified in either the organic phase or the microspheres. Thus, claim 22 further limits claim 21 by specifying that these microspheres are constituted in a majority of the polymer, and withdrawal of the objection is respectfully requested.

Claims 32 and 33 were objected to for being of improper dependent for being substantial duplicates.

These claims are amended in a manner consistent with the original claims, i.e., claim 32, refers to the polymer and claim 33 refers to the (pharmaceutically) active ingredient.

Thus, withdrawal of the objection is respectfully requested.

Claim 37 was rejected for failing to further limit claim 21.

As Claim 37 has been amended to be consistent with claim 21 (i.e., the expression “calibration by” has been replaced by "controlled”) withdrawal of the objection is respectfully requested.

Claim Rejections-35 USC §112

Claims 21, 32 and 33 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. This rejection is respectfully traversed for the reasons below.

Claim 21 was rejected for not providing a clear definition for “controlled laminar shearing”. However, one of ordinary skill in the art would have understood the meaning of this expression, and further in view of at least the two following facts:

1) First paragraph of page 25 of the present specification discloses "the controlled shearing is carried out by placing the emulsion in contact with a moving solid surface, the speed gradient characterizing the flow of the emulsion being constant in a direction perpendicular to the moving solid surface. Such shearing may be effected, for example, in a cell constituted by two concentric cylinders rotating relative to each other".
2) The teaching of FR 2 747 321, cited on page 2 of the of the present application, which corresponds to US 5,938,581, which specifies that "The shear is said to be controlled when, irrespective of the variation in the time of the shear rate, it passes through a maxium value which is the same for all parts of the emulsion, at a given instant which can differ from one point in the emulsion to another".

Claims 32 and 33 were rejected for not specifying the unit associated with the percentages. These claims are amended in a manner consistent with the original claims, i.e., claim 32, refers to "by weight of polymer" and claim 33 refers to "by weight active ingredient" (i.e., the pharmaceutically active ingredient).

Therefore, the claims are definite, and withdrawal of the rejection is respectfully requested.

Claim Rejections-35 USC §102

Claims 21, 25-28, 31, 34-36 an 38 were rejected under 35 U.S.C. §102(b) as being anticipated by COLLINS WO 03/106809 A1 (COLLINS). This rejection is respectfully traversed for the reasons below.

COLLINS relates to microparticles useful for treating hydrocarbon formations to inhibit scale deposits.

The microparticles of COLINS do not, however, comprise a pharmaceutically active ingredient, as recited in claim 21.

Moreover, COLLINS describes microparticles constituted by an aqueous solution of a water-soluble oil or gas field production chemical encapsulated by a degradable polymeric material prepared from a double emulsion W/O/W OR W/O/O. Thus, COLLINS fails to disclose microspheres prepared from a single emulsion, as recited in claim 21.

Therefore, a COLLINS fails to anticipate independent claim 21 (and, accordingly, all claim depending therefrom), withdrawal of the rejection is respectfully requested.

Claim Rejections-35 USC §103

Claims 21, 25-28, 31, 34-36 and 38 were rejected under 35 U.S.C. §103(a) as being unpatentable over COLLINS in view of LOBO et al. US 5,589,332 (LOBO). Claims 29 and 30 were rejected

under 35 U.S.C. §103(a) as being unpatentable over COLLINS in view of LOBO further in view of OKADA et al. US 5,643,607 (OKADA). These rejections are respectfully traversed for the reasons that follow below.

COLLINS was offered for the reasons discussed above relative to the anticipation rejection.

LOBO describes a process of making a fine photographic direct dispersion in the absence of auxiliary solvents. LOBO discloses that in order to form a fine dispersion of the organic phase having an average particle size of less than 0.5 micron, the ratio of the organic phase viscosity to the aqueous solution viscosity is more than 2.0.

OKADA describes microcapsules designed for sustained release of physiologically active peptides. These microcapsules are prepared from a W/O/W emulsion.

The position of the Official Action was that it would have been obvious for one of ordinary skill in the art to use the technique of modifying the viscosity of ratio of organic to aqueous phases taught by LOBO to improve the emulsion method of COLLINS to produce monodisperse micropspheres as claimed. OKADA was relied on for further guiding one to the features of claims 29 and 30.

However, one of ordinary skill in the art would not have considered the documents for preparing monodisperse

microspheres comprising a pharmaceutically active ingredient from a single emulsion as recited in independent claim 21, as:

- COLLINS and LOBO do not describe microspheres comprising a pharmaceutically active ingredient,
- the microspheres of OKADA and COLLINS are prepared from a double emulsion, and
- LOBO and OKADA do not suggest monodisperse microspheres.

That is, even if one of ordinary skill in the art had combined these three documents, the combination fails to suggest the claimed method.

More precisely, the claimed process provides monodisperse microspheres comprising a pharmaceutically active ingredient. The monodisperse feature allows a homogeneous release rate of the active principle (e.g., as discussed on page 1, line 30 to page 2, line 3 of the present specification). This features is also defined on page 7, lines 7-9.

The process according to the invention relies on the specific combination of two important technical features which are:

(1) the preparation of an emulsion comprising an organic phase such as the viscosity of the organic phase and the aqueous phase has a ratio of specifically from 0.1 to 10, and

(2) carrying out controlled laminar shearing.

This specific combination enables one to obtain monodisperse microspheres.

LOBO and OKADA fail to describe or suggest monodisperse microspheres, or provide any means to obtain a monodisperse microspheres. The applicant acknowledges that LOBO discloses that the ratio of the organic phase viscosity to the aueous solution viscosity should be more than 2.0, but this feature is associated with the size of the dispersed phase and no indication is provided that the ratio has or may have an impact on the monodisperse feature of the emulsion.

Therefore, COLLINS in combination with LOBO and/or OKADA fails to render obvious independent claim 21 (and, accordingly, dependent claims 25-28, 31, 34-36 and 38), and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the amendment to the claims and the foregoing remarks, this application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or

credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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